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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/905,212	07/13/2001	Venkatraman Ramakrishnan	256602000600	3863

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EXAMINER	
LY, CHEYNE D	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 11/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/905,212	RAMAKRISHNAN ET AL.	
	Examiner	Art Unit	
	Cheyne D Ly	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *5,6,8-11 and 14-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7,12 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-22* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' arguments filed August 26, 2004 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

2. Claims 1-4, 7, 12, and 13 are examined on the merits.

3. FINAL OFFICE ACTION.

CLAIM REJECTIONS - 35 U.S.C. § 112, FIRST PARAGRAPH

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 12 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. NEW MATTER REJECTION.

6. The instant rejection has been necessitated by claim amendments.

7. The broad limitation of "about 3 A", in line 3, has not been found in the instant specification. It is noted that the instant specification discloses the crystal of *T. thermophilus* having a determined resolution at 3.0 A (page 30, line 15) which is different from the broader limitation of "about 3 A." Page 13, lines 24-27, discloses the limitation of the structure of

the "crystals which resolve to a resolution of at least about 3 A" which is different from the broader limitation of "about 3A." Further, the original disclosure of "resolution better (numerically less) than about 3 A" in claim 12 is different from the broader limitation of "about 3 A" in the proposed amendment to claim 12.

LACK OF ENABLEMENT UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-4, 7, 12, and 13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a crystal structure of the *Thermus thermophilus* 30S subunit, does not reasonably provide enablement for any 30S subunit. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

10. This rejection is maintained with respect to claims 1-4, 7, 12, and 13, as recited in the previous office action mailed February 24, 2004.

11. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention,

(5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case is discussed below.

RESPONSE TO ARGUMENTS

12. Applicant's arguments have been fully considered and found to be unpersuasive as discussed below.

13. Applicant argues that "the specification is not applying the property of structural conservation of ribosomes for classification of species...applying the property of structural conservation of ribosomes of different species in terms of making crystals." Applicant cites to the specification (page 11, lines 11-23) to conclude that the "instant specification discloses how to make and use a crystal of a 30S ribosomal subunit from any prokaryotic species as encompassed by the instant claims." It is noted that the cited disclosure provides a description of means for providing crystals of *T. thermophilus* as exemplified by Examples 1-4 (pages 22-34) that are specific for *T. thermophilus*. However, Applicant does not disclose by guidance or working example for making crystals for different species based on the property of structural conservation of ribosomes. Therefore, one of skill in the art would not know how to predictably practice the claimed invention based on structural conservation of ribosomes without undue experimentation.

14. Applicant argues that "it appears though it may be unpredictable to crystallize individual proteins...Applicant notes that a crystal of an individual protein is not being

claimed...Rather a crystal of a 30S ribosomal subunit is being claimed." Further, Applicant argues that the Office's assertions apply to proteins, and it is not clear how said assertions of unpredictability apply to ribosomal subunits which are heterogenous complexes comprising protein and RNA. As concurred by Applicant, the art of crystallizing individual proteins is unpredictable. It is reasonable to expect that it would be unpredictable at best to reproduce crystals of individual proteins due to the high failure rate for proteins that are being crystallized. Applicant discloses that the 30S subunit comprises 16S RNA and 20 associated proteins. The increase in the number and complexity (20 associated proteins and 16S RNA) of the protein to be crystallized would reasonably increase the unpredictability factor, which would result in even higher failure rate for the 30S subunit proteins that are being crystallized. Therefore, one of skill in the art would not know how to predictably practice the claimed invention on any other 30S subunit without undue experimentation.

15. Applicant argues that the first crystallization of a ribosomal subunit was over twenty years ago, and ribosomal subunits from several different species have been crystallized. It is noted that references Yonath et al. (1980) and Ban et al. (1999) are not present in the instant application. Therefore, said references have not been considered as part of the response to Applicant's argument. Further, the cited references of Clemons et al. (2001), Cate et al. (1999), Clemons et al. (1999), and Tocilj et al. (1999) from Applicant's IDS describe the crystallization of ribosomal subunits of *T. thermophilus*. The cited references above do not provide support that ribosomal subunits from several different species have been crystallized as argued by Applicant. It is noted that the citation of several different references that provides crystals for ribosomal subunits of *T. thermophilus* at a rate of over twenty years

does not provide a preponderance of evidence to overcome the evidence of record which supports that protein crystallization unpredictable.

REJECTION RE-ITERATED

16. It is acknowledged that the applicant has disclosed information to enable one skilled in the art to make the crystal of the Thermus thermophilus 30 S subunit having a resolution of 3.05 A (Page 24, lines 28-30). However, it is well documented that protein crystallization is in essence a trial-and-error method, and the results are usually unpredictable (Drenth, J.). Further, as recently as November 1, 2002, Science published a New Focus article depicting the current state of the art for protein crystallization that supports the unpredictability of the art. In essences, protein crystallization is still a trial and error process because the current technology for producing protein for the crystallization process is unpredictable, which results in high failure rate for proteins that are being crystallized. Therefore, researchers continue to have trouble generating sufficient protein required for the crystallization process (New Focus, Science, 2002). In light of the difficulty of the protein crystallization process, it is, therefore, unreasonable to expect one skilled in the art to make any 30 S subunit crystal structure without undue experimentation.

DOUBLE PATENTING

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985);

In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

18. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

19. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

20. This rejection is maintained with respect to claims 1-4, 7, 12, and 13, as recited in the previous office action mailed February 24, 2004.

RESPONSE TO ARGUMENT

21. Applicant responded by stating that Applicant will submit a terminal disclaimer to disclaim any portion of a patent issuing from the present application, which would extend beyond the term of a patent issuing from the 09/904,779 application, upon notification of allowable claims in the present application. Applicant's response has been acknowledged. The instant rejection has been maintained until a timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) is filed.

REJECTION RE-ITERATED

22. Claims 1-4, 7, 12, and 13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of copending

Application No. 09/904,779 in view of Ramakrishnan et al. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant application and the copending application claim a crystal of a 30S subunit with identical unit cell dimensions. It is acknowledged that the copending application does not claim a crystal of a 30S subunit bound to a paromomycin antibiotic as in the instant application. However, the copending application discloses, "the 30S provided by Table 1 may be used to examine and determine the binding of antibiotics such as paromomycin" (page 11, lines 23-25). One of ordinary skill in the art would have been motivated to examine the specification for the types antibiotics that bind to the 30S subunit as disclosed in the copending application. "The specification can always be used as a dictionary to learn the meaning of a term in the patent claim. Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent." (MPEP § 804 (II) (B) (1)) Therefore, it would have been obvious to make of crystal of a 30S subunit bound to paromomycin of the instant application.

23. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

CONCLUSION

24. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

25. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

26. This application contains claims 5, 6, 8-11, and 14-22 drawn to an invention nonelected with traverse, filed March 31, 2003. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

27. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

28. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also

check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

29. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

30. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (571) 272-0716. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

31. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (571) 272-0722.

C. Dune Ly

11/8/04

MICHAEL P. WOODWARD
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

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